

REMARKS

Favorable reconsideration is respectfully requested in view of the foregoing amendments and the following remarks.

Claims 1, 7-9, 11-13, 16 and 18-22 are pending in this application. By this Amendment, claims 1, 8, 9 and 11 are amended, and claim 7 is cancelled. Claims 1, 8 and 9 are amended to more clearly recite the steps of the claimed method of examining schizophrenia. No new matter is added.

I. Claim Rejection Under 35 U.S.C. § 112

The Examiner rejects claims 1 and 7-9 under 35 U.S.C. § 112, second paragraph, as being indefinite. Applicants respectfully traverse the rejection.

The Examiner asserts that claim 1 recites an index in a biological sample, but does not disclose a characteristic of the biological sample that would allow a comparison of such index with that from a healthy individual or group. The Examiner further asserts that there must be some basis in the identity of individuals in claim 1, even if they are selected at random from populations of affected and healthy individuals, to allow a comparison of the index with those individuals identified as healthy or affected.

By this Amendment, claims 1, 8 and 9 are amended to delete the “index” language; to more clearly recite measuring concentrations in a biological sample of the subject, and a healthy individual or group of healthy individuals; and to more clearly recite the comparison between the ratios of the sample subject, and the healthy individual or group of healthy individuals. Accordingly, reconsideration and withdrawal of the rejection are respectfully requested.

II. Claim Rejections Under 35 U.S.C. § 103

The Examiner rejects claims 1, 7-9, 11-13, 16 and 18-21 under 35 U.S.C. § 103(a) as being unpatentable over Tsai. By this Amendment, claim 7 is cancelled, rendering its rejection moot. As to the remaining claims, Applicants respectfully traverse the rejection.

Tsai discloses measured values of D-serine concentration of the serum of patients with schizophrenia, but does not teach or suggest the measured values of D-serine concentration of a healthy individual or a group of healthy individuals.

As the attached Rule 132 Declaration indicates, at the time of filing of the present application, the only way to know whether the D-serine concentration of the serum of patients with schizophrenia was higher or lower than that of a healthy individual was to actually measure the D-serine concentration of the serum of patients with schizophrenia. Therefore, one of ordinary skill in the art would not have known that a comparison of the ratio of the D-serine concentration to the total serine concentration between patients with schizophrenia and a healthy individual or group of healthy individuals would have revealed a greater difference than a comparison between the raw value of D-serine concentration between patients with schizophrenia and a healthy individual or group of healthy individuals.

By referring to paragraph 3 on page 1086 of Tsai, the Examiner seems to argue that the formation of a ratio of D-serine/total serine is within the technical reach of one of ordinary skill in the art of data analysis, because the value of D-serine in samples will vary with the L-serine available for conversion by the serine racemase, the quantity and distribution of the serine racemase in the sample from which the D-serine has been extracted, and the amount of the

sample that is available and subjected to assay. See page 4 of the Final Office Action. However, it would not have been predictable for one of ordinary skill in the art to have determined whether the division of the value of D-serine by a specific value of total serine reduces or increases the error in view of Tsai.

Moreover, Snyder (Neurochemical Research, Vol. 25(5), 2000, pp. 553-560), which was cited by the Examiner in the May 28, 2008 Office Action, teaches that serine racemase has a function not only to convert L-serine to D-serine, but also to convert D-serine to L-serine. See Snyder, page 556, right column, 10th line from the bottom. Therefore, D-serine is in equilibrium with L-serine, which means, for example, that when the level of D-serine decreases, the level of L-serine also decreases.

However, Applicants have surprisingly and unexpectedly found that the D-serine concentration in patients with schizophrenia is lower than in healthy individuals and, conversely, that an L-serine concentration in patients with schizophrenia is higher than in healthy individuals. Accordingly, the D-serine concentration in patients with schizophrenia is significantly lower than in healthy individuals, and a ratio of the D-serine concentration to the total serine concentration in patients with schizophrenia is significantly lower than in healthy individuals.

As is shown in Table 1 of the present specification, the p-value for the difference of D-serine concentration between a group of healthy individuals and the group having schizophrenia is 0.001, whereas the p-value for the difference of a ratio of D-serine/total serine is below 0.0001. When the ratio of D-serine/total serine is employed, the p-value becomes 1/10 or below. This shows that the diagnosis of schizophrenia using the ratio of the D-serine concentration to the

total serine concentration is far more accurate than the diagnosis based on the D-serine concentration alone. This is both surprising and unexpected, and would not have been obvious to one of ordinary skill in the art from Tsai.

Accordingly, claims 1, 8 and 9 would not have been rendered obvious by Tsai. Claims 11-13, 16 and 18-21 depend directly or indirectly from claims 1, 8 and 9 and, thus, also would not have been rendered obvious by Tsai. Accordingly, reconsideration and withdrawal of the rejection are respectfully requested.

The Examiner rejects claim 22 under 35 U.S.C. § 103(a) as being unpatentable over Tsai as applied to claim 21, and further in view of Watanabe et al. (JP 61-080051) (“Watanabe”). Applicants respectfully traverse the rejection.

The arguments regarding Tsai discussed above are also relevant to claim 22. As discussed above, claims 1, 8 and 9 would not have been obvious over Tsai. Claim 22 depends indirectly from claims 1, 8 and 9 and, thus, also would not have been obvious over Tsai. Accordingly, reconsideration and withdrawal of the rejection are respectfully requested.

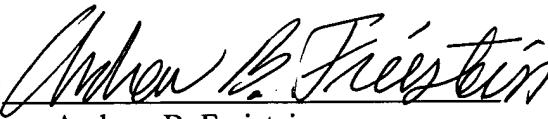
III. Conclusion

In view of the foregoing, it is respectfully submitted that this application is in condition for allowance. Favorable reconsideration and prompt allowance of claims 1, 8, 9, 11-13, 16 and 18-22 are earnestly solicited.

Should the Examiner believe that anything further would be desirable in order to place the application in better condition for allowance, the Examiner is invited to contact the undersigned at the telephone number set forth below.

Respectfully submitted,

Kenji HASHIMOTO et al.

By: 

Andrew B. Freistein
Registration No. 52,917
Attorney for Applicants

Enclosure: Rule 132 Declaration

WMC/ABF/vah
Washington, D.C. 20005-1503
Telephone (202) 721-8200
Facsimile (202) 721-8250
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